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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/870,128	05/30/2001	Oystein Ihle	4290-4000	6505

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EXAMINER	
CALAMITA, HEATHER	
ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 08/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/870,128	IHLE ET AL.	
	Examiner	Art Unit	
	Heather G. Calamita, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *39-96* is/are pending in the application.

4a) Of the above claim(s) *59-61 and 94-96* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39-58 and 62-93* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 11/26/2001, 11/7/2002
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. 07/15/2005
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

8.00

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I claims 39-58, 62 and 80-93 in the response filed on May 16, 2005 is acknowledged.

Applicant's arguments have been fully considered but they are not persuasive. Traversal was on the grounds that the subcombination of invention II must be shown to have utility either by itself or in other and different relations." The applicants assed that invention II cannot be used independently of invention I. Claim 59 recites that molecules are tagged and that "separation of tagged and untagged molecules" occurs. Claim 39 recites that molecules are tagged and that "tagged molecules are captured by the matrix and thereby separated from untagged molecules." Therefore both claims 39 (invention I) and 59 (invention II) are directed to the separation of molecules by the use of tags and should not be classified as separate inventions. The examiner maintains that the combination as claimed does not require the particulars of the subcombination as claimed because the method for separating the nucleic acid molecules can be carried out without necessarily utilizing the phage packaging technique as evidenced by claim 39 which performs the method without using the phage. Additionally, the subcombination has separate utility such as use as a packaging and delivery vector as evidenced by claim 59 which does not require all of the elements of claim 39.

Applicants argue both claims 39 and 59 utilize the procedure of separating tagged and untagged molecules. This argument is irrelevant with respect to restriction of combinations and subcombinations. MPEP 806.05 (c) states:

The inventions are distinct if it can be shown that a combination as claimed:

(A) does not require the particulars of the subcombination as claimed for patentability (to show novelty and unobviousness), and

(B) the subcombination can be shown to have utility either by itself or in other and

different relations.

When these factors cannot be shown, such inventions are not distinct.

These criteria are clearly met. As stated above the method of separating nucleic acid molecules is carried out without necessarily utilizing the phage packaging technique (see instant claim 39). Further the subcombination has separate utility as a packaging and delivery vector.

The examiner maintains the restriction requirement made previously, as each group is correctly separated as unrelated or patentably distinct and the restriction is herein **made final.** Claims 59-61 and 63-79 are withdrawn from further consideration by the examiner, 37 CFR 1.14(b), as being drawn to a non-elected invention. Pending claims to be examined are claims 39-58 and 80-93.

Priority

2. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in United Kingdom on November 30, 1998. It is noted, however, that applicant has not filed a certified copy of the 9826247.0 application as required by 35 U.S.C. 119(b).

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 39, 43, 44, 55, 56 and 62 are rejected under 35 U.S.C. 102(b) as being anticipated by Ji et al. (USPN 5,591,84, 01/07/1997).

Ji teach (claim 39) a method for at least partially separating nucleic acid molecules in a sample into populations wherein a population is tagged or capable of being tagged with a protein capable of being

immobilized on a matrix, wherein the tag interacts directly with the matrix the method comprising contacting the nucleic containing sample with a matrix whereby the tagged molecules are captured by the matrix and thereby separated from untagged molecules (see col. 3 lines 55-67).

With regard to claim 43, Ji teach the matrix is in the form of filters, membranes and columns (see col. 14 lines 15-18).

With regard to claim 44, Ji teach the matrix is a porous material (see col. 4 lines 17-18).

With regard to claim 55, Ji teach the nucleic acid molecules are separated into linear and circular DNA molecules (see col. 3 lines 55-67).

With regard to claim 56, Ji teach further comprising introducing a tag to an end of the linear nucleic acid molecules, wherein said tag is capable of being immobilized on a matrix, by direct interaction with the matrix or by indirect interaction by means of a binding partner to the tag, and contacting the sample with a matrix or, where the tag interacts indirectly with the matrix, with the binding partner to the tag and with a matrix, whereby said tagged linear nucleic acid molecules are immobilized on the matrix (see col. 3 lines55-67 and col. 8 lines 30-33).

With regard to claim 62, Ji teach a method of separating linear from circular nucleic acid molecules in a sample said method comprising introducing a tag to an end of a linear nucleic acid molecule, wherein said tag is capable of being immobilized on a matrix, by direct interaction with the matrix or by indirect interaction by means of a binding partner to the tag, and contacting the sample with a matrix or, where the tag interacts indirectly with the matrix, with the binding partner to the tag and with a matrix, whereby said tagged linear nucleic acid molecules are immobilized on the matrix (see col. 3 lines55-67 and col. 8 lines 30-33).

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 45, 46, 80-86 and 93 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ji et al. (USPN 5,591,84, 01/7/1997) in view of Seed (EP 0580305 A2, 01/26/1994).

The teachings of Ji et al. are described previously.

Ji et al. do not teach the matrix is incorporated into a separation device.

Seed teaches a matrix for separating nucleic acids is incorporated into a cartridge separation device (see example 1 lines 26-40). Additionally Seed teaches an absorbent pad is located on said porous material, a liquid impermeable sheet is located on the face of said absorbent pad remote from said porous material, and a liquid impermeable sheet having one or more holes therein is located on the face of said porous material remote from said absorbent pad, whereby the test sample is applied to one of said holes and is caused to diffuse transversely through said porous material by absorption into said absorbent pad (see example 1 lines 26-40).

One of ordinary at the time the invention was made would have been motivated to apply the method of separating nucleic acids as taught by Ji et al. with the cartridge housed matrix as taught by Seed in order to increase the convenience and efficiency with which DNA is separated. Seed states, "This example demonstrates the use of coated substrates to purify plasmid DNA from rapid lysates....The resulting suspension was transferred to a cartridge similar to that described in example 1, except that the cartridge also contained a cylindrical bundle of PHS-coated axially oriented polyester fibers... (see example 10 line 13-14 and 27-31)." Ji et al state, " it is envisioned that any support that can be retrieved after triplex formation and that is capable of immobilizing and displaying an attached duplex-binding probe for affinity capture would be adequate (see col. 4 lines 15-18)." It would have been prima facie obvious to apply the method of separating nucleic acids as taught by Ji et al. with the cartridge

housed matrix as taught by Seed in order to increase the convenience and efficiency with which DNA is separated. A single use cartridge housing the streptavidin bound matrix would be easy to store and use as exemplified by Seed.

3. Claims 47-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ji et al. (USPN 5,591,84, 01/7/1997) in view of Davis et al. (WO 90/12115, 10/18/1990)

The teachings of Ji et al. are described previously.

Ji et al. do not teach PCR of the separated DNA fragments or separation restriction fragments. Ji et al. do not teach detection of mutations in the amplified fragments.

Davis et al. teach PCR of DNA fragments and detection of mutations in the amplified fragments (see abstract, p. 24-31).

One of ordinary at the time the invention was made would have been motivated to apply the method of separating nucleic acids as taught by Ji et al. with subsequent PCR and mutation detection as taught by Davis et al. in order to rapidly identify mutations in target DNA fragments. Ji et al. state, "The entire capture and recovery process described above can be accomplished in under 30 minutes, yielding DNA that may be used directly in subsequent molecular-biological processes (see col. 8 lines 38-42)." Ji et al. give examples of these processes as restriction enzyme digestion, cloning and DNA sequencing (see col. 8 lines 26-27). Davis et al state "By using the methods and products of this invention, it is possible to determine the genotype of an individual at any locus of interest. A single nucleotide position on a strand of DNA may be responsible for polymorphism or allelic variation. There are known disease states that are caused by such variation at a single nucleotide position. The usefulness of detecting such variation inculudes but is not limited to gene typing, karyotyping, genotyping, DNA family planning, diagnostics...(see p. 1). It would have been prima facie obvious to apply the method of separating nucleic acids as taught by Ji et al. with subsequent PCR and mutation detection as taught by

Davis et al. in order to rapidly identify mutations in target DNA to use in applications such as for example, diagnostics, genotyping and prenatal testing.

4. Claims 57 and 58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ji et al. (USPN 5,591,84, 01/7/1997) in view of Dower et al. (USPN 5,427,908, 06/27/1995).

The teachings of Ji et al. are described previously.

Ji et al. do not teach invitro packaging into bacteriophage particles.

Dower et al. teach invitro packaging into bacteriophage particles (see abstract).

One of ordinary at the time the invention was made would have been motivated to apply the method of separating nucleic acids as taught by Ji et al. with invitro packaging into bacteriophage as taught by Dower et al. in order to rapidly screen a DNA library of interest. Dower et al. state "Methods are needed which facilitate the screening process, thereby enabling DNA sequences which encode proteins of interest and particularly antibody molecules to be more readily identified, recloned and expressed (see col. 1 lines 36-40)." It would have been prima facie obvious to apply the method of separating nucleic acids as taught by Ji et al. with subsequent invitro packaging into bacteriophage as taught by Dower et al. in order to rapidly screen a DNA library of interest.

5. Claims 40-42 and 89-92 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ji et al. (USPN 5,591,84, 01/7/1997) in view of Wagner, Jr. (USPN 6,120,992, 09/19/2000).

The teachings of Ji et al. are described previously.

Ji et al. do not teach a nucleic acid binding protein.

Wagner teaches Mut S, a nucleic acid binding protein (see abstract).

One of ordinary at the time the invention was made would have been motivated to

apply the method of separating nucleic acids as taught by Ji et al. with a nucleic acid binding protein as taught by Wagner, in order to isolate DNA of interest. Wagner states, "The present inventor has conceived of the use of compositions and methods which employ immobilized mismatch binding proteins for example the Mut S protein of E. coli for the following...(2) partial or complete purification of amplified DNA samples by removing contaminating sequences and sequences containing errors introduced during the amplification processes... (see col. 6 line 67-col. 7 lines 1-3)." It would have been prima facie obvious to apply the method of separating nucleic acids as taught by Ji et al. with the nucleic acid binding protein as taught by Dower et al. in order to isolate DNA of interest away from contaminating sequences since Mut S binds DNA with a high degree of specificity.

6. Claims 87 and 88 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ji et al. (USPN 5,591,84, 01/7/1997) in view of Cotton et al. (USPN 5,698,400, 12/16/1997).

The teachings of Ji et al. are described previously.

Ji et al. do not teach digoxygenin.

Cotton et al. teach digoxygenin (see col. 3 lines 19 and 29).

One of ordinary at the time the invention was made would have been motivated to apply the method of separating nucleic acids as taught by Ji et al. with digoxygenin as taught by Cotton, in order to isolate DNA of interest. Cotton et al. state, "...the heteroduplex is tagged with at least one detection moiety; the detection moiety being...biotin; digoxygenin; a luminescent agent...(see col. 3 lines 26-29)." It would have been prima facie obvious to apply the method of separating nucleic acids as taught by Ji et al. with digoxygenin as taught by Cotton et al. in order to detect isolated DNA of interest. Digoxygenin is more convenient than radiolabels as there are no health or disposal issues with which to contend.

Summary

8. No claims are allowable.

Correspondence

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Heather G. Calamita whose telephone number is 571.272.2876 and whose e-mail address is heather.calamita@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route. The examiner can normally be reached on Monday through Thursday, 7:00 AM to 5:30 PM.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at 571.272.0782.

Papers related to this application may be faxed to Group 1637 via the PTO Fax Center using the fax number 571.273.8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to 571.272.0547.

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hgc.

JEFFREY FREDMAN
PRIMARY EXAMINER